Maastricht University

Resting-state fMRI neurodynamics in neuropsychiatric disorders

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Valorisation

Main findings

In this thesis, new ways of modelling brain dynamics using functional magnetic resonance imaging (fMRI) are described. A measure of causality, synchronicity, and emulative power between resting-state brain networks were assessed in two clinical populations: autism adolescents and elderly with accelerating cognitive ageing (ACA). The main findings are: (i) time of in-phase coherence extracted from wavelet coherence approach, i.e. the measure of synchronicity between brain networks, is a good descriptor of the autistic disorder, and allow the fMRI-based diagnosis of autism with high accuracy (> 85%); (ii) the evolutionary game theory approach and its derived emulative power between brain networks combined with wavelet coherence, Granger causality, and static functional connectivity approaches could classify ACA from non-ACA with more than 95% accuracy; (iii) Granger causality gives relevant information about the direction of the brain network connectivity involved in the deficiency displayed in autism or ACA, but is not a strong biomarker (classifiers fell short of providing high accuracy performances), whereas a new Bayesian topology modelling for describing causality in the brain dynamics seems to have added value (compared to Granger causality) and should be explored further.

Relevance

Mental disorders are estimated to be prevalent in 18% of Dutch population (18 to 64 years old), with the most commons psychological disorders being: depression, specific phobia, social phobia, alcohol abuse and ADHD, according to the Dutch organisation of mental health (GGZ [1]). And even though mental health problems are the major cause of burden of disease, mental health providers only use 6.1% of total health and social care budget, in the Netherlands. Unfortunately, in addition, treatments for neuropsychiatric patients are known to be often ineffective due to misdiagnosis or the poorly understood aetiology of the conditions. Two solutions can be proposed for tackling these issues: allocating more healthcare and social care budgets for research in psychiatry, or distributing these resources in a more optimal way, i.e. with advances in techniques that ensure reliable diagnoses and treatment effect prognostics.

Knowing more about the mechanisms of action of a mental disorder can greatly help with avoiding misdiagnosis and designing targeted and more effective treatment solutions. The findings of the research presented in this thesis are actually relevant for psychoradiology, the field of research studying psychology through the lens of brain images; and hence, relevant for advancing the study of brain pathologies, and more specifically, the (neuro)psychiatric disorders. Therefore, if this research is pushed forward with better understanding of the pathological brain dynamics, treatment that would target and affect these dynamics can be developed; and misdiagnoses may be also avoided.

[1] https://www.denederlandseggz.nl/

In addition, this research allows the follow-up of the progression of neuropsychiatric disorders by helping in screening the brain dynamics changes and/or through visualisation and analysis of treatment effects, using fMRI scans.

Overall, advances in psychoradiology, as presented in this thesis, can be relevant and beneficial for the healthcare system with regard to mental health and its cost-efficient budget allocation.

Target groups

This research is not only relevant for the field of psychoradiology and its societal effect on the healthcare system. Indeed, this thesis is directly targeting patients with autism and elderly with cognitive decline problems. And more generally, the research also aims at improving the lives of patients with neurological or psychological disorders, since these new methods for assessing brain dynamics could be used for understanding mechanisms of action of other mental disorders.

In addition to the patients, clinicians can profit from this type of research and development by having new tools to assess brain disorders; and brain dynamics visualisation and understanding can facilitate the diagnosis or the prediction of treatment response in case of neurological or psychiatric conditions. This research has, overall, the potential to re-assure objectively clinicians' decisions regarding the diagnosis of a disorder or the prescription of therapies.

Furthermore, another target group that would benefit from this research may be new service developers. Startups such as Icometrix[2] or Advantis[3] can very much be interested in new features allowing the visualisation of cognitive processes and descriptive markers of disorders, when structural imaging and other anatomical markers are not sufficient.

Finally, not only startups in post-processing image-based diagnostics but also MRI scanner vendors (e.g. Philips, or Siemens) could use the results presented in this thesis for new products. Indeed, this research and the impact it can have on the healthcare system and brain-diseased patients may incentivise vendors to develop more precise and specific hardware together with advanced MRI sequences for extracting robust neuropsychological brain markers.

Activities and products

As mentioned in the previous paragraph, new companies are being developed to offer services helping clinicians in the decision-making process for diagnosing brain conditions; and vendors of MRI scanners could incorporate the methods for accessing brain dynamics described in this thesis in their clinical and research software. These new tools would allow radiologists and clinicians to have a quicker and insightful look into the brains of the scanned patients. These critical insights put in clinical practice would alleviate the issue of misdiagnosis, and can also reassure the clinicians in their decisions (regarding diagnosis and treatment). So, new products can be developed from this neuroimaging research: e.g., brain dynamics visualisation software or reliable biomarkers extraction tools. Combining these products could lead to a strong computer-aided automated diagnostic tool.

[2] https://icometrix.com/
[3] https://advantis.io/

One activity we could think of is to integrate these new brain dynamics extraction methods into existing brain visualisation and analytic software (e.g. BrainVoyager[4], or the FSL software package[5]. Another activity could be to patent the process of diagnosis/prognosis of a disease: from the scanning protocol and image processing pipeline to the automated classification and description of a patient's condition. Similar ideas of image-based technology for prediction of diseases has already got granted patents (e.g. Siemens' patent US7949167B2).

This research can also be extended to the study of more localized and deeper neuronal dynamics. Indeed, the findings of this thesis could be utilised for reading brain signals extracted from more advanced imaging techniques, such as brain-chip neural recording. For example, Neuralink[6] is making great advances in neuronal recording and stimulation, which can provide a clearer (than the currently-used fMRI and EEG techniques) picture of activity in the brain. This research could greatly help to decipher and disentangle the dynamics of the large neuronal time-series data at a finer scale (than large-scale network dynamics observe in behaviour and cognition). This can help to design new solutions to restore functions in neurologically impaired patients (e.g. restoring sight, hearing, or motor control).

Innovation, future work and implementation

This thesis contains innovation for analysing brain dynamics. So far, brain fMRI images were assessed through correlation, giving clinicians and researchers static maps and metrics of brain network topology. Now, with novel insights into the dynamic processes of the brain, we saw that the brain functional topology can evolve. And most pathologies reside and can be described in this dynamic topology. In addition, this view of assessing the communication between large-scale networks, rather than within all possible connections, is novel. It simplifies substantially the complexity of the models, but also allows understandable conclusions regarding abnormal brain connectivity—it is easier to describe high-level communication mechanisms to understand behavioural issues rather than modelling complex neuronal connectivity that hardly explains the emergence of pathological cognition and behaviours.

More innovation could be made in the data acquisition, with multi-modal techniques for instance. Coupling the high temporal resolution of an EEG and the high spatial resolution of MRI scans could extend the range of products and commercial activities for modern psychoradiological tools. Mixing structural data from diffusion-weighted imaging with fMRI-based brain features could also improve models for neuropsychiatric classification.

The development of these new tools, products and activities for neuropsychiatric diagnosis, or visualisation software for treatment strategies could be clinically implemented. However, before having these diagnostic and visualisation tools implemented in clinical practice, the research in psychoradiology for neuropsychiatric disorders must be consolidated. Fortunately, more and more research institutes provide the world with open access, and freely available anonymised datasets (e.g. OpenNeuro[7] and HCP[8] repositories (. However, these medical imaging data centres are usually constituted of anatomical brain images; but once similar data centres provide brain functional MRI data of neuropsychiatric patients and controls, more research will be conducted to improve and refine the models presented in this thesis. This will ultimately lead the neuropsychiatric field towards personalised (and disease-specific) diagnostic and treatment solutions.

[4] http://www.brainvoyager.com/
[5] https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/
[6] https://neuralink.com/
[7] https://openneuro.org/
[8] http://www.humanconnectomeproject.org/

We could expect machine learning applications for the detection of robust biomarkers of neuropsychiatric to be developed in the coming decade. This time-frame is not unrealistic, since machine learning and AI algorithms are being developed currently in the field of medicine. Plus, this research in neurodynamics using fMRI can be easily performed in parallel with neuropsychological clinical evaluation practices. Indeed, the idea for further development is to simply add one or two MRI scanning sessions to the already performed surveys and psychological evaluations. And this add-up in the evaluation of neuropsychiatric disorders does not enlarge the burden of the patients and clinicians; whereas it actually enlarges the data collections in the data centres aforementioned, and hence, the research possibilities. Moreover, all the analytic research and data collection can be done at relatively no cost—if radiological costs are traded off with better targeted treatments— which is of benefit for the healthcare system and the society. Finally, machine learning data service startups, and scanner vendor companies could see, in these neuroimaging technologies, a great opportunity to developed further and for a broader costumer audience their commercial activities in healthcare and mental well-being.